

the penetration and localization of the anesthetic and analgesic agents relative to conventional topical preparations such as ointments and creams.

Claims 1-11 are directed to the method for providing local anesthesia and analgesia, whereas claims 12-15 are directed to a pharmaceutical composition containing lipid vesicles with specifically enumerated local anesthetic agents and analgesic agents encapsulated therein.

Claim 1 is rejected under 35 USC §102(a) as being anticipated by Janoff U.S. 4,721,612 and claims 1-15 are rejected under 35 USC §103 as being unpatentable over Janoff '612 in view of Haynes U.S. 4,725,442. These rejections are respectfully traversed.

Janoff '612 pertains to the preparation of liposomes (lipid vesicles) by employing a salt form of an organic acid derivative of a sterol, such as the tris-salt form of a sterol hemisuccinate. The modified-sterol liposomes are particularly useful for administering entrapped compounds in vivo. Janoff, at Col. 10, lines 50-65, provides a shotgun disclosure of 31 different classes of biologically active compounds that can be entrapped using his modified-sterol liposomes. Local anesthetics are one of the enumerated classes. Janoff also discloses the full gambit of administration routes at Col. 10, lines 66 to Col. 11, line 7, including the use of topical application. Janoff does not, however, specifically suggest or disclose using topical application of liposomes containing a local anesthetic, and particularly does not recognize that enhanced penetration and localization is obtained with this method of administration. Consequently, a rejection under §102 of the statute is not well-founded.

Janoff does present one example using an analgesic-type drug. In Example 10.1, Janoff describes the intramuscular injection of liposomes containing indomethacin.

Like Example 10.1, all of the other Examples also are directed to the use of injection as the mode of administering the liposomes containing the biologically active or pharmaceutical compounds. Janoff does not present a single example using his liposomes for topical application of a drug.

Even if Janoff '612 makes it *prima facie* obvious to topically apply liposomes containing an anesthetic or analgesic agent, applicants' surprisingly unexpected showing in the patent application that enhanced penetration and localization is obtained by this method of treatment, effectively rebuts such a *prima facie* case.

In Example 10.3, Janoff also presents evidence showing that his particular liposomes are different from liposomes made using conventional phospholipids. Thus, there is at least a suggestion that his liposomes behave differently from those made using conventional ingredients and procedures. Claims 7-11 of the subject application are directed specifically to liposomes made from conventional phospholipids.

Haynes '442 specifically relates to a method for obtaining local anesthesia by intradermal or intravenous injection of general anesthetics, and broadly pertains to the injection of other water-insoluble anesthetics or drugs using microdroplets smaller than one micron having a phospholipid monolayer. Haynes' microdroplets are not liposomes. Thus, Haynes does not disclose incorporating local anesthetics such as benzocaine into a liposome.

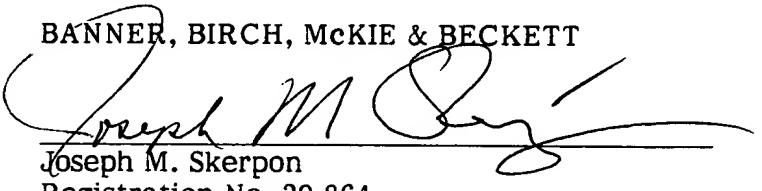
If anything, Haynes underscores Janoff's lack of a specific teaching to administer local anesthetics topically using liposomes. Surely, Haynes, which is devoted specifically to the injection of general and local anesthetics would not make it obvious to depart from that administration procedure when employing Janoff's liposomes, particularly where Janoff in all his Examples, including one of an analgesic-type drug,

also employs injection techniques. Applicants' surprising discovery that topical application of such local anesthetics and analgesic agents, particularly those identified in claims 3, 10 and 12, entitles applicants to a patent for their discovery.

Reconsideration of the pending application is respectfully requested.

Respectfully submitted,

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